Intravenous Administration of Fat Emulsions

Metabolic and Clinical Studies

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• Fat emulsions alone or in alternation with amino acid mixtures were administered by continuous intravenous infusion to human subjects. Adequate nutrition was maintained thereby, without untoward effects. Upon too rapid administration of such emulsions, toxic manifestations occurred, apparently referable to an "overload" of the enzyme systems concerned with fat catabolism and storage.

THE TWO MATERIALS available for parenteral feeding are sugars and protein hydrolysates. With neither of these is it possible to maintain caloric and protein equilibrium in a person who has to subsist entirely on parenteral feeding over a long period, for the unhappy choice is between giving so concentrated a solution that sclerosis of the veins results, or so dilute a solution that the patient literally may be drowned if attempt is made to administer as much as 1,800 calories daily.

The solution to the problem lies in the availability of a fat emulsion suitable for intravenous use. A variety of such emulsions have been prepared and have been evaluated in animals and humans, but have been found to be unsuitable for general clinical application because of either "breaking" of the emulsion or the presence in the emulsion of materials that are toxic to the recipient.[1, 2, 3, 4, 5]

During the past year the authors have evaluated several small lots of fat emulsion prepared by the Research Department of Armour Laboratories. These emulsions had been shown to be highly stable, and to produce essentially no toxic manifestations in laboratory animals when infused at a reasonable rate.

Chart 1 gives data on the initial study—the infusion of 400 cc. of a 10 per cent emulsion over a two-hour period into a patient who was under study on the metabolic ward. In a clinical sense the infusion was completely uneventful. Chemically it was noted that the neutral fat content in the plasma had reached approximately 800 mg. per 100 cc. at the end of the infusion, and that the level fell rapidly after the infusion was completed. A very slight elevation of blood ketones was also noted, and a significant decrease in the iodine number of the plasma. The decrease in iodine number presumably was referable to the dilution of endogenous plasma lipids with the infused material, which was low in unsaturated fatty acids.

The next study (Charts 2 and 3) was carried out as a two-day balance procedure in a patient who was

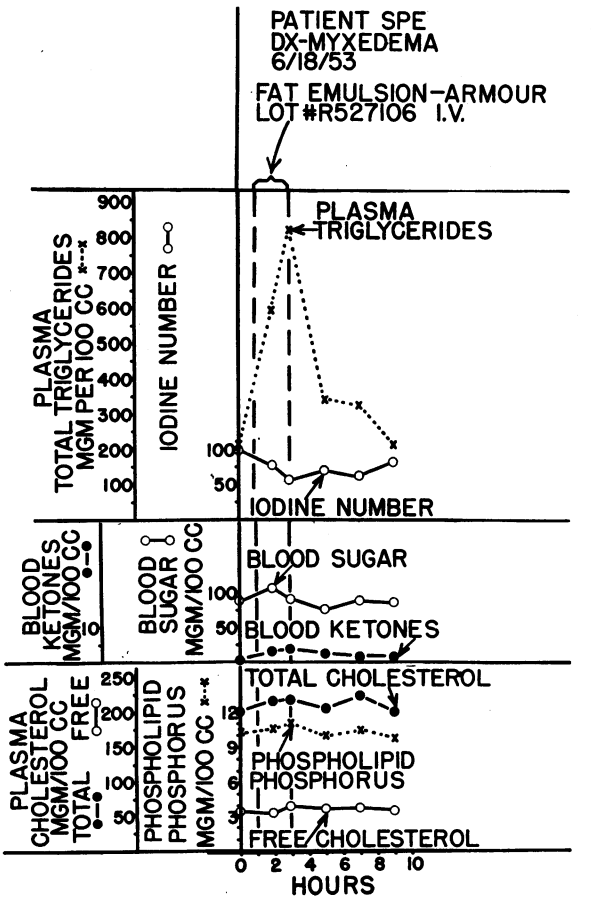

Chart 1.—Infusion of fat emulsion (20 gm. of fat per hour) for a two-hour period, brought about a rapid rise in plasma triglycerides but no untoward clinical effects.

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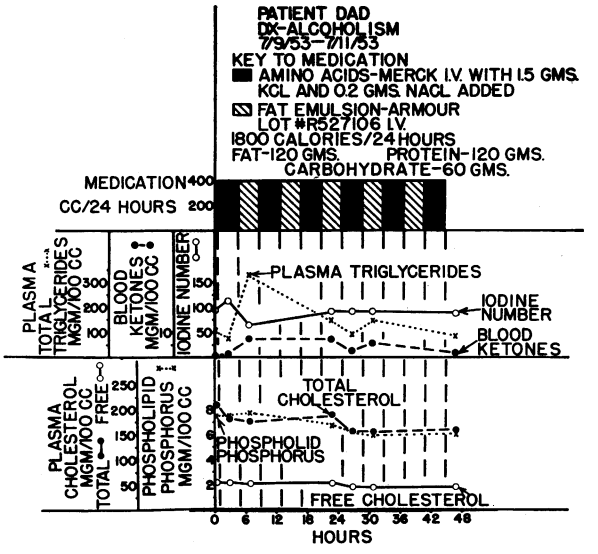

Chart 2.—Alternate infusion for four-hour periods of 100 cc. of 10 per cent fat emulsion (plus 5 per cent glucose) and 10 per cent amino acid mixture, is well tolerated clinically and biochemically.

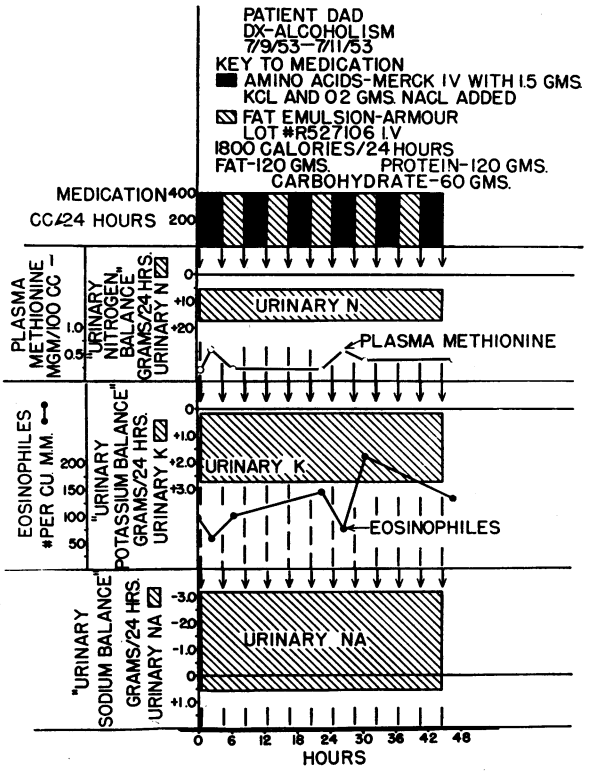

Chart 3.—The infusion referred to in Chart 2 resulted in a strongly positive nitrogen balance throughout a 48-hour period. The reason for the sodium diuresis is unknown.

recovering from an alcoholic episode. The fat emulsion was infused intermittently with a 10 per cent amino acid mixture, each being administered at the rate of 100 cc. per hour. It will be noted in the charts

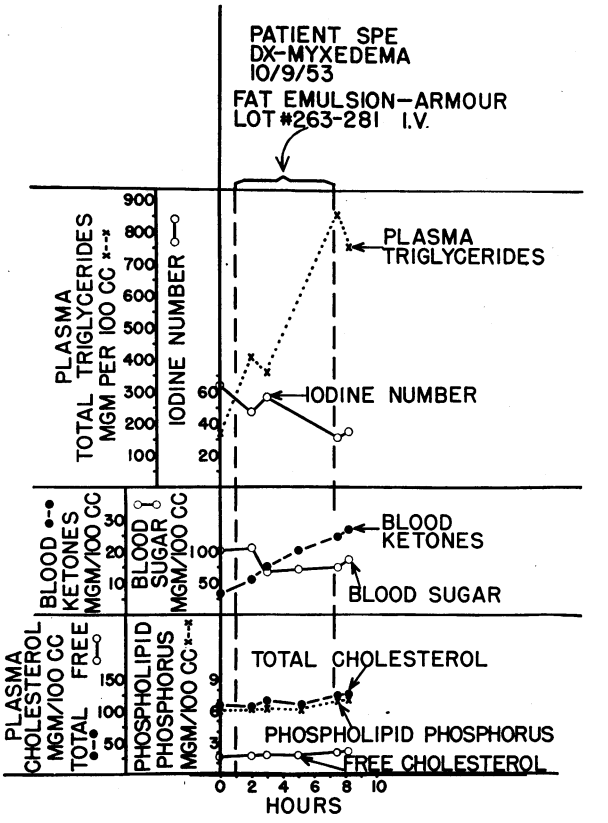

Chart 4.—Infusion of a 10 per cent fat emulsion at a rate of 20 gm. of fat per hour for a six-hour period resulted in a rapid rise in plasma neutral fat and blood ketones, and eventually in production of toxic manifestations.

that the initial rise in plasma triglycerides was followed by a fall, even though the infusion continued, apparently attributable to a "compensation" of the body machinery concerned with utilization of fat. The blood ketones rose moderately and then gradually fell. During the period of infusion, the patient received 1,800 calories per day with the distribution between fat, protein and carbohydrate as shown. He was in strongly positive nitrogen balance throughout.

The next study (Chart 4) was carried out on the patient who received the initial infusion. The fat emulsion was infused at a rate of 200 cc. per hour throughout a six-hour period. Nausea, vomiting and some low back pain began approximately an hour after the infusion was completed, and continued for two hours. Temperature elevation appeared during the infusion and continued for several hours thereafter. It will be noted that under these conditions the blood ketones rose rapidly to levels of approximately 25 mg. per 100 cc. and the triglycerides to values above 800 mg. per 100 cc.

The final study (Charts 5 and 6) was of a three-day balance in an elderly man with osteoporosis. The infusion was carried out as in the first balance procedure, at the rate of 100 cc. per hour, with the

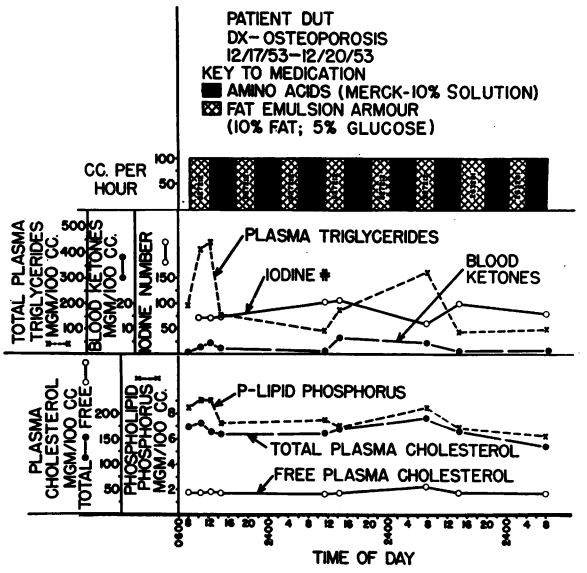

Chart 5.—Infusion carried out as in Chart 2 for a three-day period in an elderly patient was well tolerated clinically and biochemically.

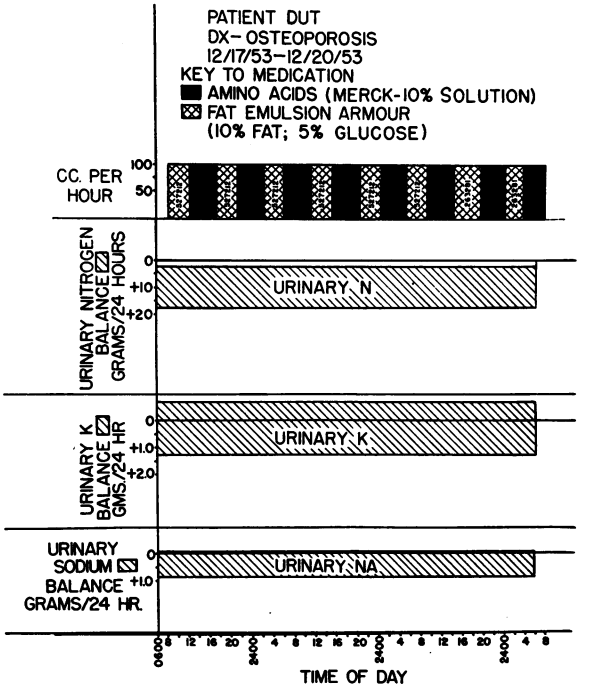

Chart 6.—Three-day parenteral feeding with alternate fat emulsion and amino acid solution resulted in a positive nitrogen balance. Potassium loss may have been related to increased urinary output.

amino acid mixture and fat emulsion alternating. The pattern with regard to plasma triglycerides and blood ketones as well as clinical status was essentially identical with that noted in the initial balance study. The patient was in positive nitrogen balance throughout.

DISCUSSION

From the foregoing, it appears that the infusion of a properly prepared fat emulsion in human subjects can result in maintenance of adequate nutrition without untoward effects. It further appears that too rapid administration of such an emulsion results in toxic manifestations, which presumably are attributable to an accumulation of fat in abnormal locations. Interference with essential metabolic processes results. Additional work will be required to determine the minimal, maximal and optimal tolerance in terms of grams of fat per kilogram of body weight. On the basis of clinical and biochemical data so far available, the infusion of 20 grams of fat per hour for six hours exceeds the tolerance of an adult of average size, but 10 grams per hour is well tolerated.

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